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APPENDIX
(REDACTED INVENTION DISCLOSURE)

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INVENTION DISCLOSURE

PAGE ONE OF ____

NO 10010218 DATE RCVD [redacted] ATTORNEY MJB

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scriptive Title of Invention:

icro-fluidic flow switching device

ime of Project:

icro Analytical Technologies

oduct Name or Number: n/a

as a description of the invention published, or are you planning to publish? If so, the date(s) and publication(s):

o

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'as the invention disclosed to anyone outside of AGILENT TECHNOLOGIES, or will such disclosure occur?. If so, the date(s) and name(s)

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'as the invention described in a lab book or other record? If so, please identify (lab book #, etc.)

088-46,47,48,49,53,54,55

'as the invention built or tested? If so, the date:

es, [redacted]

'as this invention made under a government contract? If so, the agency and contract number:

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escription of Invention: *Please preserve all records of the invention and attach additional pages for the following. Each additional page should be signed and dated by the inventor(s) and witness(es).*

A. Prior solutions and their disadvantages (if available, attach copies of product literature, technical articles, patents, etc.).
B. Problems solved by the invention.
C. Advantages of the invention over what has been done before.
D. Description of the construction and operation of the invention (include appropriate schematic, block, & timing diagrams; drawings; samples; graphs; flowcharts; computer listings; test results; etc.)

ignature of Inventor(s): I (we) hereby submit this disclosure on this date: [[redacted]].

Employee No.	Name	Signature	Telnet	Mailstop	Entity & Lab Name
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[redacted]	Hongfeng Yin	[signature]	[redacted]		[redacted]

(If more than four inventors, include additional information on another copy of this form and attach to this document)

Form 3.1 IDF1016.DOC Rev[redacted]

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nature of Witness(es): *(Please try to obtain the signature of the person(s) to whom invention was first disclosed.)*
invention was first explained to, and understood by, me (us) on this date: [redacted]

Name	Signature	Date of Signature
Tom A. van de Goor	aaavan	[redacted]
harmila R. Udiavar	SUdiavar	[redacted]

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Invention Disclosure

Micro-fluidic flow switching devices

Kevin Killeen and Hongfeng Yin, Agilent Labs, [redacted]

Background

Micro-fluidic (μ-fluidic) devices hold great promises for many applications. One of the most critical μ-fluidic elements is a low dead volume, reliable and leak free flow switching element (valve). Applications such as sample introduction, step gradient and linear gradient liquid chromatography (LC), the introduction of reagents into a flow stream, and the selection from different flow streams and/or fraction collection into different fluidic chambers etc. all require a valve to be successfully practiced.

Prior Art

Valve structures generated by silicon micro-machining technologies are described in US Patent Nos.: 4,768,751; 5,725,017; 5,964,239; 5,927,325; 6,102,068; 5,771,902; 5,333,831; 5,368,704; 5,417,235; 5,819,749; and 4,869,282. Laser ablated butt-coupled rotor-stator valve design has been described in US patent Nos.: 5,500,071; 5,568,413, and 5,571,410.

Summary of the invention

The present invention relates to a micro machined flow-switching device for use in micro fluidic applications. In the preferred embodiment of the present invention, two micro fluidic substrates form a high pressure capable, face seal rotary valve where fluidic structures on both devices are in fluidic communications with each other. Flow path switching is achieved with actuation and rotation of one substrate relative to the other with the capability to connect multiple flow channels sequentially or simultaneously. In another embodiment, one of the substrate is simply a rotor seal or binary shut off valve. In another embodiment, at least one of the substrates can be connected to external fluid source. An alternative embodiment would be a relative displacement (linear or combination motion e.g. slide valve), rather than just rotary motion between elements. This valve concept is extensible to multiple micro fluidic valve elements sandwiched between layers of m-fluidic structured channels.

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The actuation of the valve is via mechanical coupling to a motor or pneumatically driven shaft. Alternatively, by choice of proper materials, the valve material itself may be driven by magnetic or electrical forces for non-contact actuation.

The materials of construction used in the present embodiment are low cost polymers, specifically commercial grade polyimide (Kapton™) and PEEK (polyetherether ketone). These materials can be processed by tool machining, laser ablation and plasma etching to form μ-fluidic structures in surfaces. PEEK can also be embossed or injection molded to define fluidic features. Elements constructed from alternative polymer and/or solid materials combinations are possible if they are chemically compatible with the fluids in contact with them, can withstand the internal pressures of the application without fatigue or leaks, and are mechanically stable to wear during repetitive actuation of the valve. A reliable seal between the moving elements is enhanced by using (a) compliant material(s) with the deformation of one element relative to the other forming a leak tight structure statically and during actuation.

A commercial ten-port valve design has been used to test operation in both the flow injection analysis (FIA) mode and step gradient LC mode . In step gradient mode, one loop is loaded with sample and the other loop is loaded with high percentage organic mobile phase. By switching between the two positions, sample is first loaded during the time that the LC column is flushed with mobile phase A. Then, the valve is switched. Now, sample is injected onto the LC column and non-retaining compounds are eluted by mobile phase A while Loop B is loaded with mobile phase B. Then the valve is switched again, and mobile phase B in loop B is pushed through LC column and sample is eluted through ES spray tip into Mass Spectrometer.

Functions that can be addressed by the face seal rotary valve design:

1. High pressure (>250 bar), low dead volume, leak free, simultaneous or sequential connection of muliple flow paths.
2. Fixed loop microinjection of sample for FIA mass spec analysis (commonly practiced with a 6-port design)
2. Fix loop injection for step gradient LC separation (10-port design as described above)

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3. Fix loop sample injection for true gradient LC (6-port design, also with switching of splitting point)
4. Multi-position selection valve for sample selection, fraction collection and flow diversion
5. Multiple-switching with single actuation, rotor seal can address multi-channel simultaneously or actuator can address multi-rotor seals simultaneously.
6. Shut-off valve to allow or stop flow between fluid paths connected via the rotary seal.
7. Sequential switching design between differing flow paths to generate a LC gradient on chip.
8. Multilayer, stacked valve elements sandwiched between u-fluidic layered structures.

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LC-MS Chip

The "*KEY*" Chip

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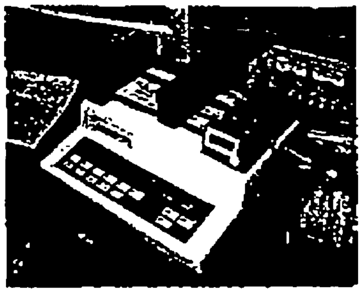
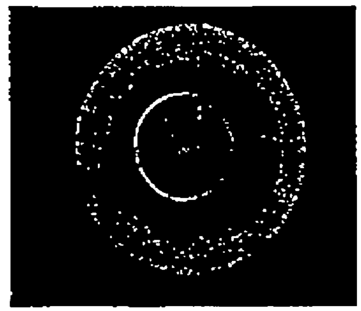
Essential Elements of the *Key* Prototype

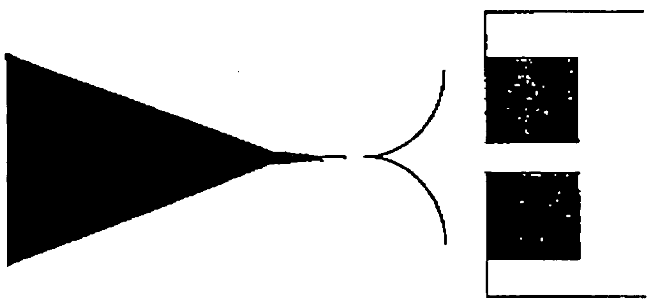


pump



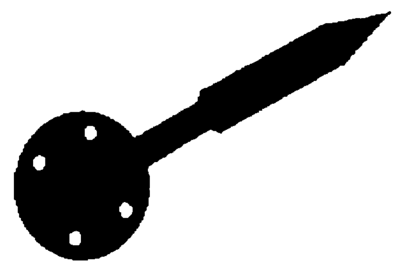
valve

column



detector

(ESI-MS)



HP, LDV connections

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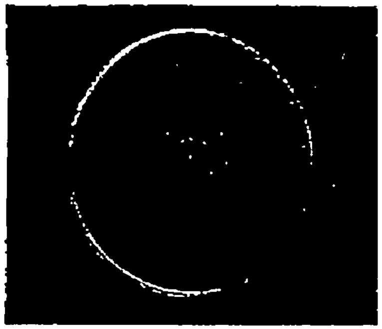
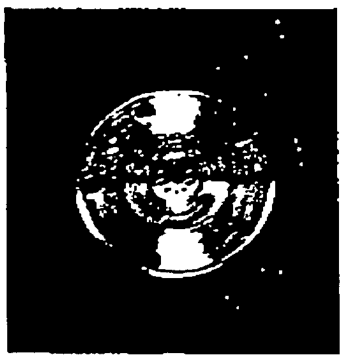
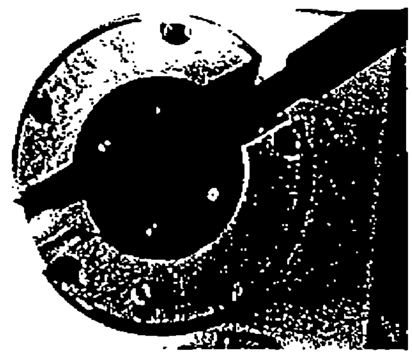
Valve to Chip Interface



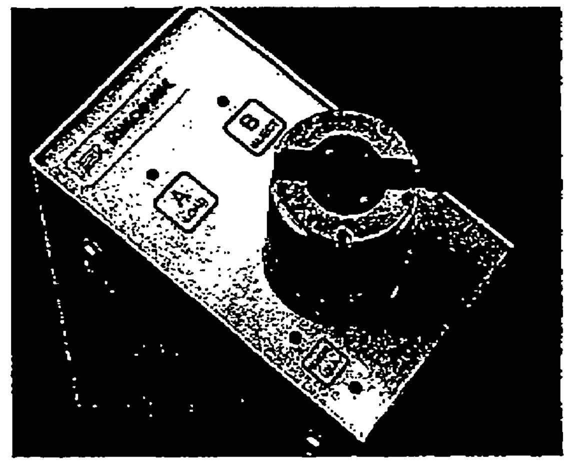
1 nl, laser ablated PEEK rotor loops



Inside face of 10 port SS stator



Kapton *Key* chip face sealed between rotor and stator. Tested to 250 Bar.



Flow switching using 2 position actuator

Switching by valve motion

Mechanical actuation vs. electrical switching for CE or CEC

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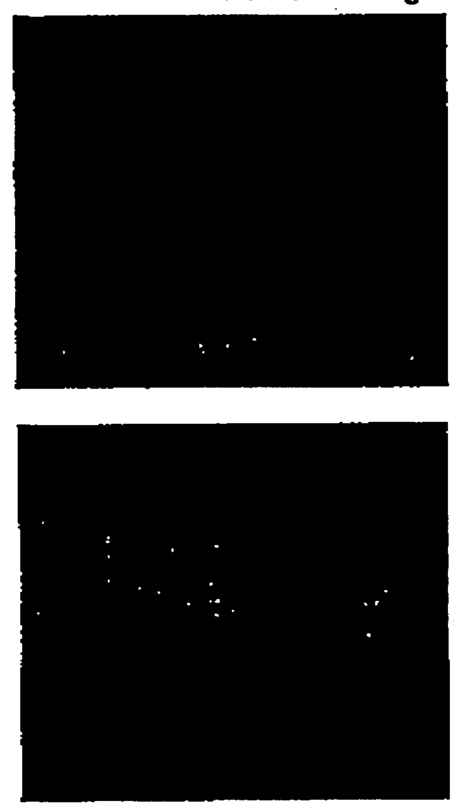
LC Column Packing

Industry-standard Packing / LC Chemistry:

Proven LC technologies and methodologies

Reflection image



5 µm bead diameter

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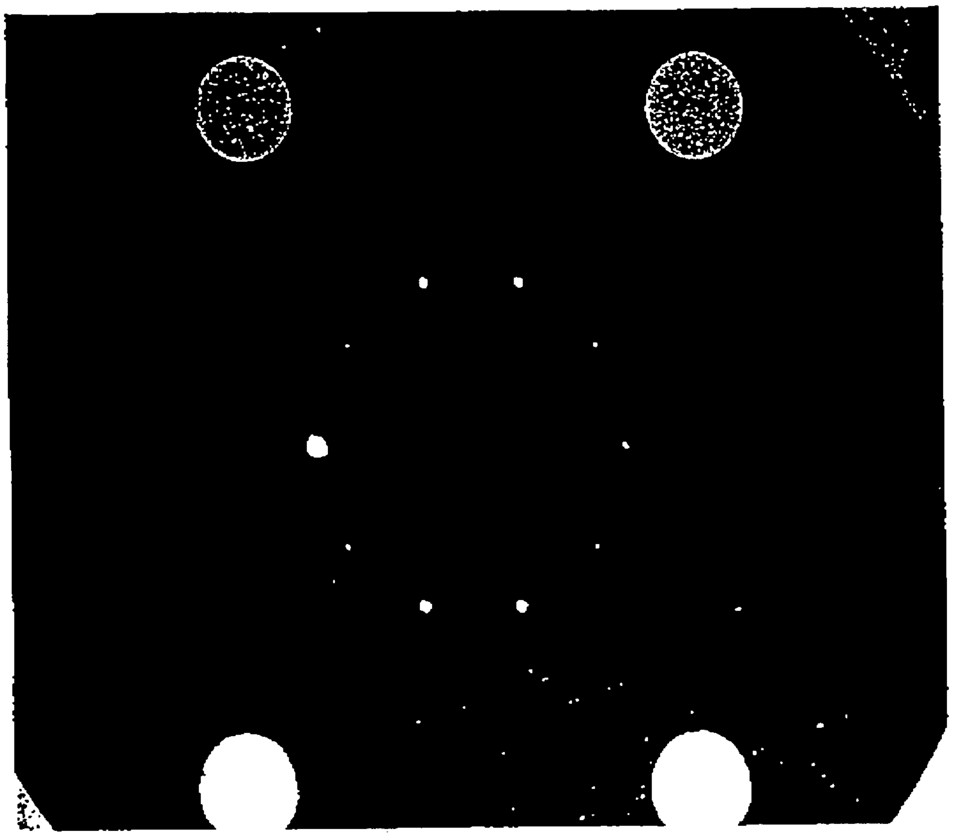
KEY Chip Layout



Sample loop = 11.2 nl
Loop B = 26.6 nl
Column Volume before packing = 27.3 nl

Integrated on-chip sample loop, mobile phase B loop, LC column, and flow switching means

Low dead and delay volume, fast separation and washout, low carry-over

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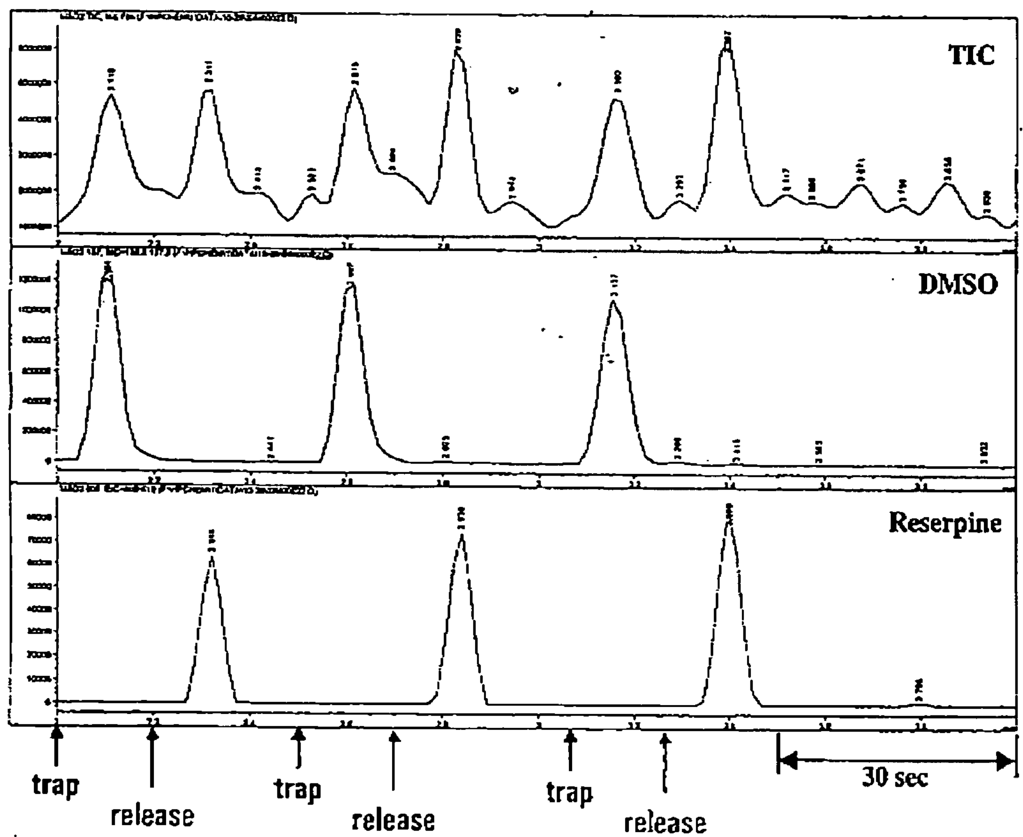
Fast Clean-up

Remove DMSO interference from Reserpine



Experiment condition:
MS: Sprite single Q MS, scan 70 – 650 amu
Sample: 1ug/ml reserpine in 0.1% DMSO, 10 pg injected
Mobile phase A:
10% Methanol/Water, 0.5% formic acid
Mobile Phase B:
90% Methanol/Water, 0.5% formic acid
Flow rate: 1ul/min
Injection: 10nl loop
B loop: 25nl
Step Gradient:
0 min. inject sample, load loop B
0.2 min flush column with B, new sample loaded
0.5 min inject new sample

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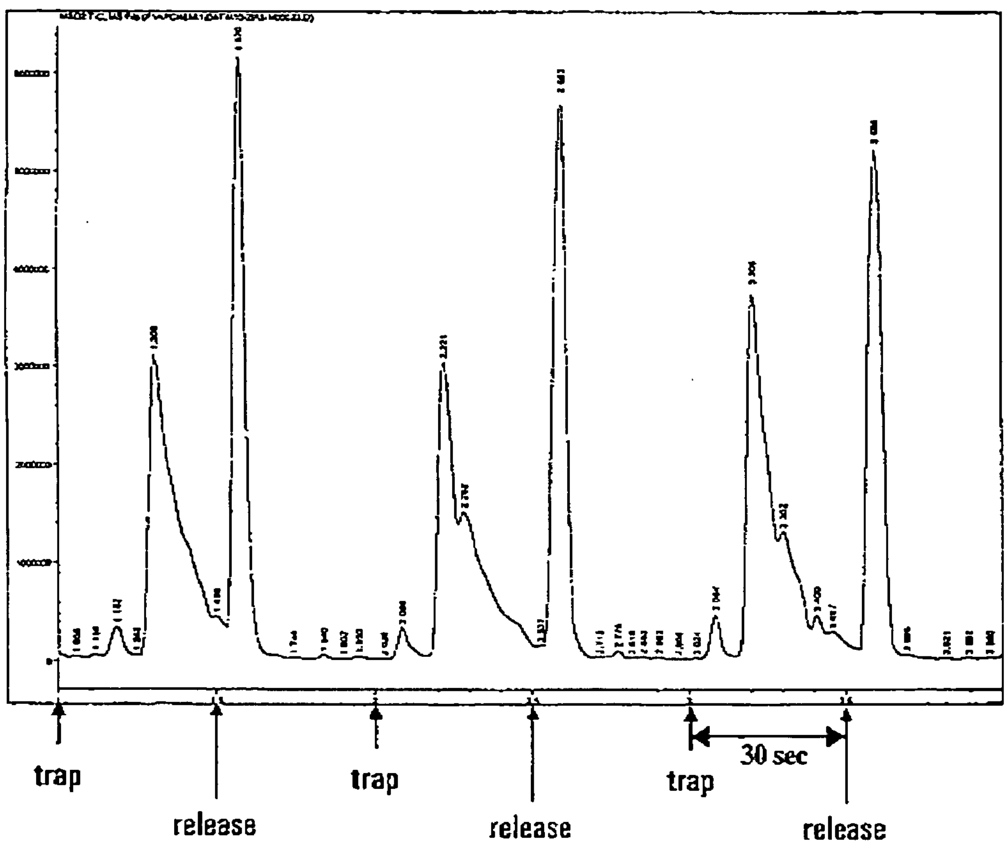
Step Gradient LC-MS

Clean-up and separation of peptide mixture



Experiment condition:
MS: Sprite single Q, scan 250-900 amu
Sample: Sigma LC peptide mix
Mobile phase A:
10% Methanol/Water, 0.5% formic acid
Mobile Phase B:
90% Methanol/Water, 0.5% formic acid
Flow rate: 1ul/min
Injection: 10nl loop
B loop: 25nl
Step Gradient:
0 min. inject sample, load loop B
0.5 min flush column with B, new sample loaded
1.0 min inject new sample

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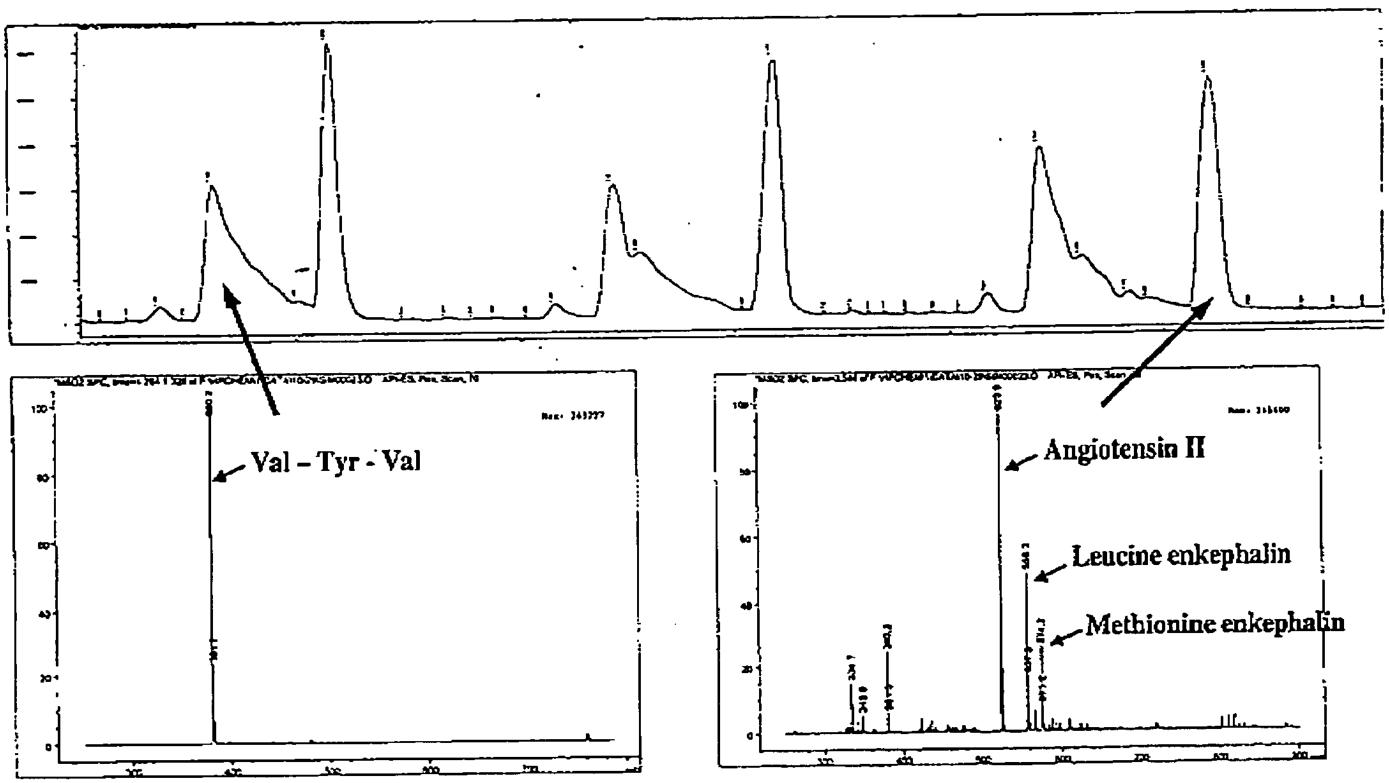
Step Gradient LC-MS

Clean-up and separation of peptide mixture



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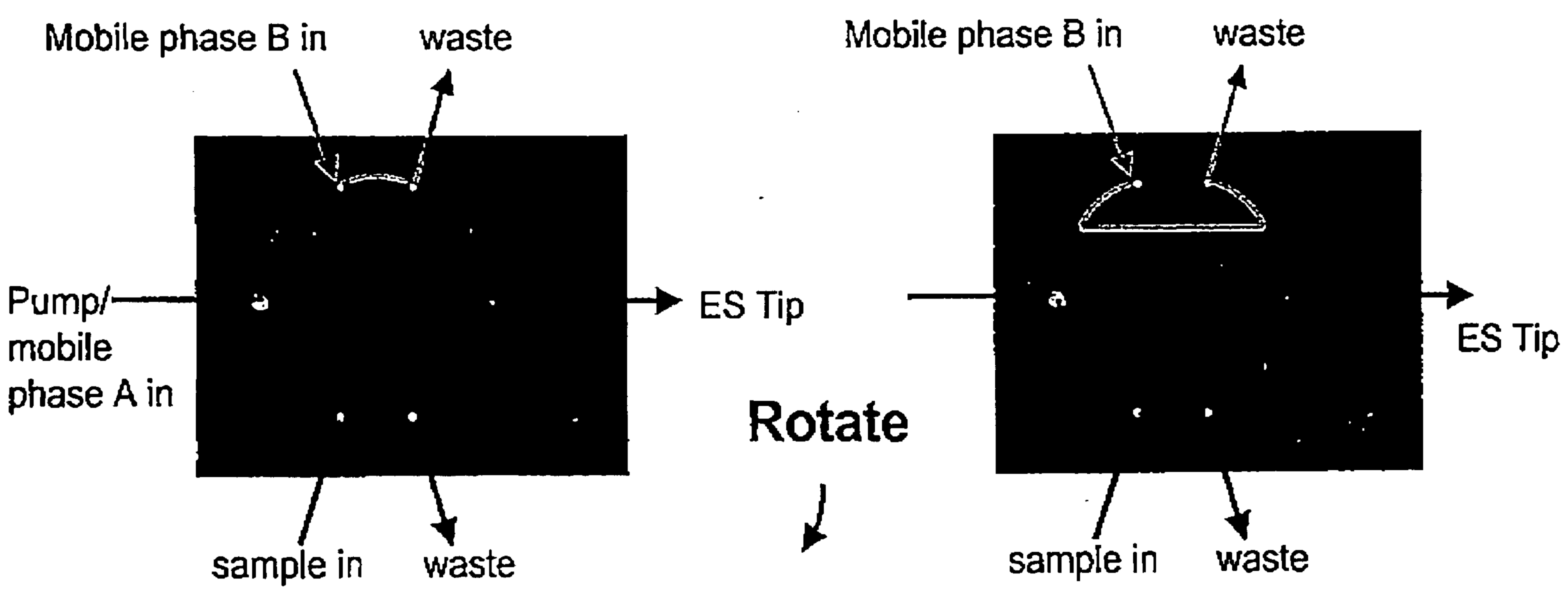
Flow Switching and Sample Injection for Step Gradient LC



Sample Loop Fill

Inject

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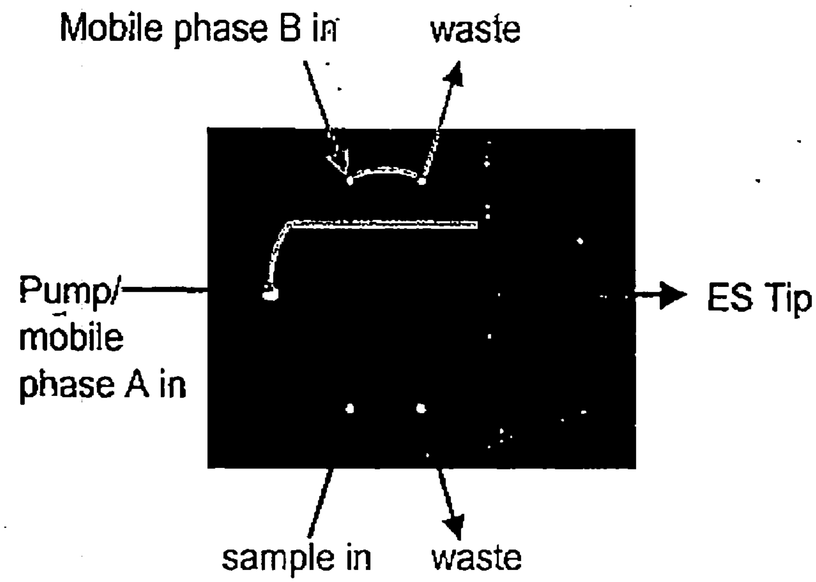
Flow Switching and Wash for Step Gradient LC

Rotate



Sample Wash (Elute)

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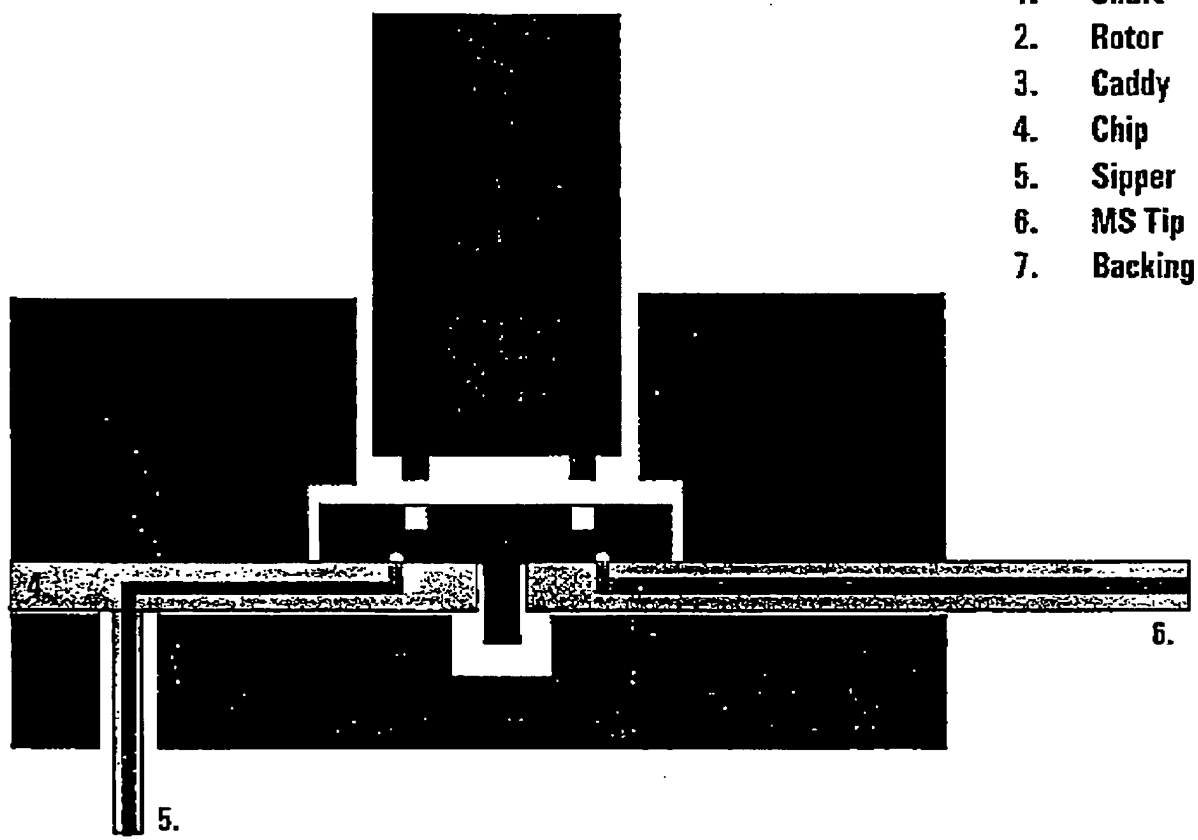
LC-MS Concept

1. Shaft
2. Rotor
3. Caddy
4. Chip
5. Sipper
6. MS Tip
7. Backing



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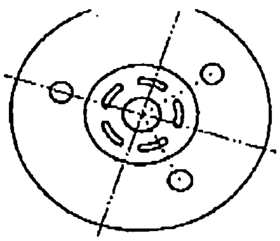
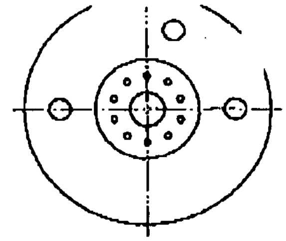
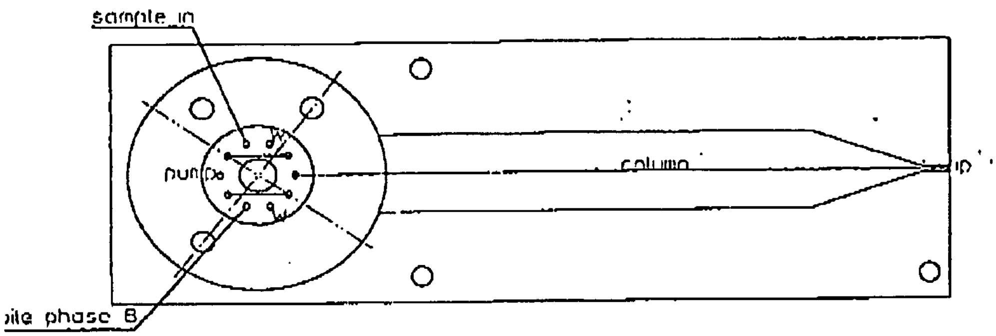
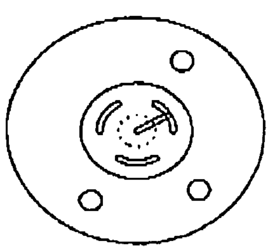


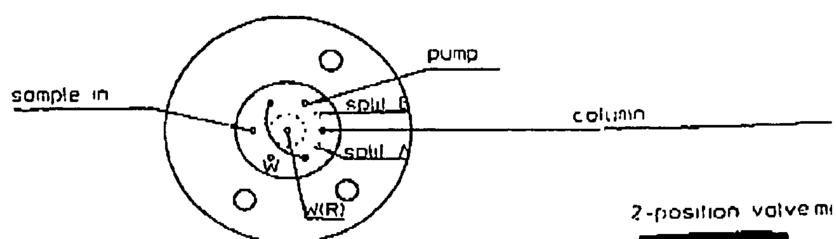
Rheodyne rotor seal



Rheodyne stator face assembly







2-position valve m

[redacted]

Hongfeng Yin

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